Neural connectivity as revealed by SEF wave shape: A morphological MEG study

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1 Introduction

The time varying spatial properties of the evoked cerebral response to external stimuli depicts the characteristics of the excited neural circuitry for the specific sensory involved modality. These spatiotemporal features are reflected in the shape of the brain evoked response, and our aim is to quantitatively characterize individually anatomo-functional features for the somatosensory system (somatosensory evoked fields = SEFs). Suitable tool could be magnetoencephalographic (MEG) signal, being not distorted by the extra-cerebral layers (i.e. the skull and meninges) separating neural currents from the recording apparatus: this allows the waveform of the evoked response to directly describe the spatio-temporal cerebral activation.

The morphology of SEFs following median nerve stimulation has been described as two initial peaks of opposite polarity (M20, M30, around 20 and 30 ms from the stimulus onset, [1, 2, 3, 4]), followed by a third component between 50 and 100 ms from the stimulus onset. Despite this pattern, the shape of the response is quite variable from subject to subject. In fact, great inter-individual variability has been previously described recognizing three morphology categories for the latter component ([4], for our data, Fig1): in some subjects it has the same polarity as the preceding one (Fig. 1, S1, 61% of our cases), in others it shows the opposite (Fig. 1, S2, 29% of cases) or is even absent (Fig. 1, S3, 10% of cases).

Combined with this inter-individual variability of SEF morphology, a great intra-subjective, inter-hemispheric similarity of SEF pattern is evident (Fig. 1). Moreover, SEF morphology is very stable when tested in successive independent sessions in the same subject. Our study attempts to define a parameter that describes intra-subject inter-hemispheric similarity, quantitatively evaluates it in a healthy population and calculates its normative limits.

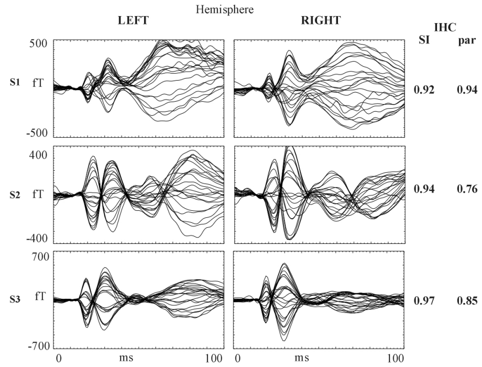

Figure 1: *Superimposition of all recording channels in left/right parietal regions (respectively left/right columns) in the 100 ms post-stimulus period. SEFs of three paradigmatic subjects are presented, to show different SEF morphologies (compare S1, S2, S3 in one hemisphere) both in the time intervals before 45 ms and between 45 and 100 ms from the stimulus onset. By comparing SEF from left vs right hemisphere for each subject, the intra-subject inter-hemispheric shape similarity is appreciable. On the right side, their parameters values are reported (IHC_SI, IHC_par).*

2 Methods

2.1 Subjects and recording procedures

In 22 healthy volunteers the SEF morphology has been studied following electrical separate stimulation of left and right median nerve. MEG recordings were performed in a magnetically shielded room (Vacuumschmelze GMBH) both by a 28-channel system at the Fatebenefratelli Hospital in Rome, which covers a scalp area of about 180 cm^2 (centering the recording apparatus on the C3/C4 positions of the 10-20 International EEG system) and by a 165-channel helmet system at ITAB – University of Chieti. This system features 153 integrated magnetometers (8x8 mm^2 area) evenly distributed over the whole scalp, plus 12 channels for noise reduction. The overall system noise is better than 5 fT/Hz^{½} above 1 Hz.

The analysis of morphological properties has been performed, in order to quantify the inter-hemispheric correlation within the same subject and to identify SEF morphology classes, to which a single individual could belong. For these purposes a parameter able to quantify the similarity of intra- or inter-subjects SEF morphology is proposed.

2.2 Morphological analysis

The wave shape analysis focused separately on SEF short-latency components before 45 ms from the stimulus onset (M20, M30) and on the later component between 45 and 100 ms. They were treated independently as first components are the most stable and independent of subject's attention; in the meanwhile the later one shows higher variability across different subjects. Moreover the first two components are known to be generated at the primary sensorimotor cortex only contralateral to the stimulus; the later, generated in the posterior parietal cortex, have been otherwise described by some authors as bilateral [5] and by others only contra-lateral to the stimulus [3]. The analysis started with M20 onset and correlated signals in a 30 milliseconds time interval; the second interval started from the end of this first and included the following 50 ms. The alignment of left and right responses at the M20 onset was chosen to focus on waveform comparative analysis only for the time following the arrival of sensory input to the primary sensory cortex (M20 component, generated in SI).

The shape analysis comparing SEF morphologies in the two hemispheres was conducted by as described in Fig. 2:

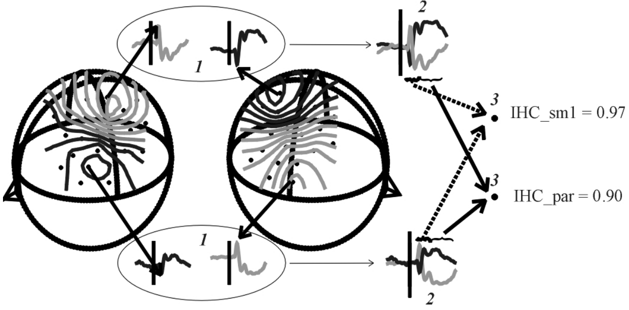

Figure 2: *Description of the parameter chosen to evaluate the SEF shape correlation in the two hemispheres: the two channels with opposite polarity and maximal amplitude in each hemisphere were selected (1); the correlation coefficients between each of the two channels in one hemisphere and the one in the corresponding cerebral region of the other hemisphere were calculated (2) and these two correlation indexes were averaged (3) in each time period (the first 30 ms from the M20 onset (=IHC_SI), and the following 50 ms (=IHC_par)).*

Once the parameter values in the 22 subjects were calculated, normative one-tailed thresholds were calculated including 98% of the control population. The parameter distribution did not result in gaussian-shaped and the following transformation allowed us to achieve the best fit: y = ln(1-x), where x=IHC_SI (or IHC_par). Therefore, the normative lower limit was calculated as

$$1 - exp(mean(y)+z_{0.98}*st.dev(y)).$$

3 Results

3.1 Wave shape characteristics

The wave shape analysis in the period including M20 and M30 components showed a remarkably elevated inter-hemispheric shape similarity with an average IHC_SI = 0.96, consistent with a symmetrical intra-subjective activation spatio-temporal profiles of the examined ECDs in the two hemispheres (Fig. 1 comparing left and right hemispheres in 3 paradigmatic subjects). When considering the later components, the related IHC_par parameter also showed the high 0.94 average value, although with larger variability.

3.2 Normative values

The normative limits, including 98% of the control population, resulted in 0.76 and 0.54 for the two parameters IHC_SI and IHC_par respectively. Wave shapes from the two hemispheres resulting in IHC_SI and/or IHC_par below the normative limits should therefore be considered abnormally asymmetric, as related to primary somatosensory areas and/or parietal ones. These parameters are useful to test eventual alterations in the activation properties in patients affected by a mono-hemispheric cerebral lesion or an unilateral alteration of the sensory inflow from hand district.

4 Discussion

The evaluation of the activation properties of the somatosensory cortical areas provides a more deep understanding of the anatomical-functional substrate in the human cerebral processing of the sensory information from the hands. Shape similarities that we observed in SEF recordings in response to sensory stimulation of different hand districts (median nerve and fingers) underline the connection between the anatomical-functional neural substrate of the cortical relay activation profiles on one side and the evoked response morphology on the other.

The inter-hemispheric SEF correlation parameters might provide useful information to detect unilateral abnormalities in the activation pattern as consequence of a cerebral lesion, or when unilateral peripheral inflow alterations occur. As we have shown, the intra-subject inter-hemispheric correlation is very high in healthy humans and it is for this reason a powerful abnormality index. This could help in clinical conventional sensory testing that is often insufficient to assess precisely the amount of the patient's sensory dysfunction following an hemispheric lesion [6,7]; meanwhile, the estimation of discriminative sensory impairment is important because subtle sensory disturbances might be related to clinical outcome.

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